Citation:

Mutungi G, Ratliff J, Puglisi M, Torres-Gonzalez M, Vaishnav U, Leite JO, Quann E, Volek JS, Fernandez ML. Dietary cholesterol from eggs increases plasma HDL cholesterol in overweight men consuming a carbohydrate-restricted diet. *J Nutr.* 2008 Feb;138(2):272-6.

PubMed ID: 18203890

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To compare the effects of a Carbohydrate Restricted Diet (CRD) high in cholesterol (provided by eggs) to the one low in cholesterol (using an egg substitute) on the variables of metabolic syndrome
- Hypothesis is that including eggs in the CRD would not alter the beneficial effects of the CRD on plasma lipids and body composition

Inclusion Criteria:

No list of inclusion criteria described.

Recruitment took place at the University of Connecticut and surrounding areas

- 31 men enrolled
- Ages between 40-70 years old
- BMI range 26-37 kg/m^2

Exclusion Criteria:

- Hypothyroidism
- Documented Heart Disease
- Type 1 Diabetes
- Gout
- Egg allergies

Description of Study Protocol:

Recruitment

Recruited from the University of Connecticut (Storrs, CT) and surrounding areas.

Design: Parallel, randomized, placebo-controlled trial

Blinding used (if applicable)

Single blinded. Liquid egg and cholesterol/fat free eggs (egg substitute) were purchased from Vistar. The substitute had the same color and consistency as the eggs. Subjects did not know which group they were assigned to.

Intervention (if applicable)

- All subjects were free living and followed a CRD for 12 weeks. Energy intake was not restricted
- Carbohydrates were restricted to 10-15% of total energy, 25-30% protein, 55-60% fat.
- Measurements of blood samples, body composition, food records, blood pressure and anthropometrics were collected at baseline, week 6, week 12
- Physical activity was recorded at baseline and each week during the intervention. They were asked to maintain normal routine of physical activity throughout the study.
- Subjects received weekly follow-up counseling where body mass and compliance was measured. Further dietetic education was provided at this time
- Three day food records were obtained at baseline. Five day records were completed during weeks 1, 6 and 12.
- Subjects were given specific instructions regarding the types of foods that must be avoided on a CRD and they could not consume additional eggs beyond what they were given,
- There was no restriction on the types of fats consumed.

Statistical Analysis

- Dietary assessment analyzed using Nutritional Data System 5.0 (University of Minnesota)
- Mean values were obtained for nutrient intake at each data collection point
- Obtained values for total energy, absolute and percent contribution from macronutrients were obtained; dietary fats and cholesterol were calculated.
- Two way repeated measures ANOVA were used to determine diet effects and time effects on plasma lipids, food intake, body composition, and blood pressure.
- $P<0.05$ was considered significant
- Data reported as means±SD

Data Collection Summary:

Timing of Measurements

- 12-hour fasting blood samples, body composition, food records, blood pressure and anthropometrics were collected at baseline, week 6 and week 12
- Three day weighed food records were obtained at baseline
- Five day food records were completed during weeks 1, 6, 12 of intervention

Dependent Variables

- Blood values for total cholesterol, triglycerides, LDL-C, HDL-C and plasma glucose
- Anthropometrics -
    - weight measured to the nearest 0.5 lb

- height measured to the closest 0.5 inch
- BMI calculated as kg/m^2
- waist circumference measured mid-way between the lowest rib and iliac crest to the nearest 0.1cm

- Blood pressure - measured on the right arm after 5 minutes of rest; measured twice by the same individual during the same week to account for variability
- Body composition
  - body mass measured in the morning after an overnight fast
  - body mass recorded to the nearest 100g on a calibrated digital scale with subjects wearing only underwear
- Whole body and regional composition was assessed using dual-energy x-ray absorptiometry (DEXA)

Independent Variables

- Carbohydrate restricted diet
- Egg or egg substitute

Control Variables

Description of Actual Data Sample:

Initial N: 31 males

Attrition (final N): 3 dropped out due to compliance issues; final N=28

Age: 40-70 years old

Ethnicity: not described

Other relevant demographics: none described

Anthropometrics BMI 26-37 kg/m^2. Groups did not differ in anthropometrics and blood pressure at baseline.

Location:Storrs, CT at the University of Connecticut and surrounding community

Summary of Results:

Key Findings:

- Energy intake decreased in both groups from 10,243 ± 4040 to 7968 ± 2401 kJ ($P < 0.05$) compared with baseline.
- All subjects irrespective of their assigned group had reduced body weight and waist circumference ($P < 0.0001$).
- Similarly, the plasma triglyceride concentration was reduced from 1.34 ± 0.66 to 0.83 ± 0.30 mmol/L after 12 weeks ($P < 0.001$) in all subjects.
- The plasma LDL-cholesterol concentration, as well as the LDL-C:HDL-C ratio, did not change during the intervention.
- In contrast, plasma HDL-C concentration increased in the EGG group from 1.23 ± 0.39 to 1.47 ± 0.38 mmol/L ($P < 0.01$), whereas HDL-C did not change in the SUB group.

- Plasma glucose concentrations in fasting subjects did not change

Changes in Plasma Lipids, LDL-C:HDL-C Ratio, and Glucose at Baseline, 6 and 12 weeks

	Baseline Measures and confidence intervals	Week 12 Measures and confidence intervals	Statistical Significance of Group Difference
Total Energy, kJ/d	2544±921	1962±691	<0.05
--EGG group	2318±1030	1821±408	
--SUB group			
Carbohydrates, %	42.4±8.3	14.9±9.3	<0.0001
--EGG group	41.5±9.5	19.9±12.1	
--SUB group			
Fat, %	39.9±7.2	56.1±10.3	<0.0001
--EGG group	39.2±8.4	54.9±13.8	
--SUB group			
Protein, %	17.1±3.7	26.9±6.5	<0.0001
--EGG group	18.6±5.9	24.5±3.6	
--SUB group			
Cholesterol, mg/d*	319±150	827±192	<0.0001
--EGG group	354±170	277±100	
--SUB group			
Body Weight, kg	98.9±15.3	92.2±12.7	<0.0001
--EGG group	97.6±19.9	91.7±15.7	
--SUB group			
Trunk Fat, %	37±7.4	31.6±8.7	<0.0001
--EGG group	38.6±6.6	32.5±8.3	
--SUB group			
WC, cm	107.9±11.6	101.5±2.7	<0.0001
--EGG group	108.8±15.8	102.1±14.7	
--SUB group			

Systolic BP, mm Hg	134.0±12.4	123.5±14.0	<0.0001
--EGG group	136.2±15.6	126.1±13.9	
--SUB group			
Diastolic BP, mmHg	85.3±5.2	74.7±7.7	<0.0001
--EGG group	82.3±8.3	77.7±5.6	
--SUB group			
Total Cholesterol, mg/dL	198.3±42.1	202.2±41.8	>0.1
--EGG group	188.3±33.7	187.3±39.5	
--SUB group			
TG, mg/dL	114.2±49.4	70.1±20.8	<0.001
--EGG group	126.1±69.4	76.7±33.0	
--SUB group			
HDL-C, mg/dL**	47.6±15.1	57.1±15.1	<0.01
--EGG group	50.0±9.7	48.8±8.8	
--SUB group			
LDL-C, mg/dL	127.5±42.2	144.3±45.1	>0.1
--EGG group	110.8±34.5	121.5±42.0	
--SUB group			
LDL-C/HDL-C	2.27±0.83	2.46±1.04	>0.25
--EGG group	2.37±1.14	2.42±0.78	
--SUB group			

- *There were no diet or diet time effects for any of the variables except for dietary cholesterol, P<0.001
- There were no differences between groups or interactions in any of the body weight, anthropometric and blood pressure variables, P>0.2
- No data was reported for physical activity
- **There were no diet or interactive effects for any of the blood variables except for HDL-C, P<0.01

Other Findings

- There were 18 subjects at baseline (58% of total) classified as having Metabolic Syndrome as defined by the National Cholesterol Education Program ATP III
- 11 were in the EGG group and 7 were in the SUB group
- Following the intervention, only 3 subjects remained in this classification and they were all from the SUB group

Author Conclusion:

CRD improve all parameters related to MetS, including plasma lipids, fasting glucose, waist circumference, and blood pressure. A challenge of dietary cholesterol during a weight loss intervention involving CRD does not alter the positive effects of a CRD on features of MetS but rather plays a major role in the positive effects on plasma HDL-C concentrations.

Reviewer Comments:

- *Funded by the Egg Board*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	???
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		???
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**		???
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	No